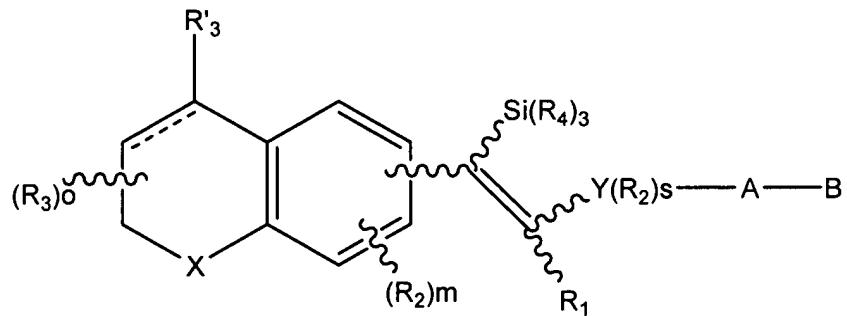


Amendments to the Claims

Please cancel Claims 8-11 and 32-40. Please amend Claims 1, 2, 5, 12, and 13. Please add new Claims 41-60. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Currently amended) A method of treating an FXR-mediated pathological condition selected from hypercholesterolemia and hyperlipoproteinemia in a mammal comprising the step of administering to a mammal in need thereof a pharmaceutically acceptable composition comprising a synthetic FXR ligand able to stimulate, block or inhibit the activity of a mammalian FXR receptor, said synthetic FXR ligand comprising a compound of the formula a compound of the formula:



formula (3)

wherein the dashed line represents a bond or absence of a bond;

X is S, O, NR' where R' is H or alkyl of 1 to 6 carbons, or X is (C(R₁)₂)n where R₁ is H or alkyl of 1 to 6 carbons, and n is an integer having the value of 0 to 1;

R₂ is hydrogen, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, CF₃, fluoro substituted alkyl of 1 to 6 carbons, OH, SH, alkoxy of 1 to 12 carbons, or alkylthio of 1 to 12 carbons, benzyloxy or C₁-C₁₂ alkylbenzyloxy;

R₃ is hydrogen, lower alkyl of 1 to 6 carbons or F;

m is an integer having the value of 0-3;

o is an integer having the value of 0-4 when the dashed line represents absence of a bond, and 0-3 when the dashed line represents a bond;

R'₃ is hydrogen, lower alky of 1 to 6 carbons, F or (R₁₅)_r-phenyl, (R₁₅)_r-naphthyl, or (R₁₅)_r-heteroaryl where the heteroaryl group has 1 to 3 heteroatoms selected from the group consisting of O, S and H, r is an integer having the values of 0-5;

R₄ is alkyl of 1 to 8 carbons, or phenyl;

s is an integer having the value of 0-2;

Y is phenyl or naphthyl group, or heteroaryl selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, imidazolyl and pyrazolyl, said phenyl and heteroaryl groups being optionally substituted with one or two R₂ groups;

R₁₅ is independently H, F, Cl, Br, I, NO₂, N(R₈)₂, NH(R₈), COR₈, NR₈CON(R₈)₂, OH, OCOR₈, OR₈, CN, an alkyl group having 1 to 10 carbons, fluoro substituted alkyl group having 1 to 10 carbons, an alkenyl group having 1 to 10 carbons and 1 to 3 double bonds, alkynyl group having 1 to 10 carbons and 1 to 3 triple bonds, or a trialkylsilyl or trialkylsilyloxy group where the alkyl groups independently have 1 to 6 carbons;

A is $(CH_2)_q$ where q is 0-5, lower branched chain alkyl having 3-6 carbons cycloalkyl having 3-6 carbons, alkenyl having 2-6 carbons and 1 or 2 double bonds, alkynyl having 2-6 carbons and 1 or 2 triple bonds;

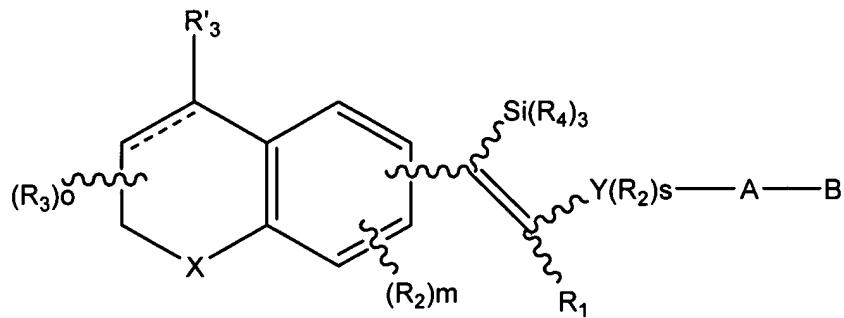
B is hydrogrn, COOH, NO₂, P(O)(OH)₂, P(O)(OH)OR₈, P(O)(OR₈)₂, SO₂OH, SO₂(OR₈), COOR₈, CONR₉R₁₀, -CH₂OH, CH₂OR₁₁, CH₂OCOR₁₁, CHO, CH(OR₁₂)₂, CHOR₁₃O, -COR₇, CR₇(OR₁₂)₂, CR₇OR₁₃O, or tri-lower alkylsilyl, where R₇ is an alkyl, cycloalkyl or alkenyl group containing 1 to 5 carbons, R₈ is an alkyl group of 1 to 10 carbons or trimethylsilylalkyl where the alkyl group has 1 to 10 carbons, or a cycloalkyl group of 5 to 10 carbons, or R₈ is phenyl or lower alkylphenyl, R₉ and R₁₀ independently are hydrogen, an alkyl group of 1 to 10 carbons, or a cycloalkyl group of 5-10 carbons, or phenyl or lower alkylphenyl, R₁₁ is lower alkyl, phenyl or lower alkylphenyl, R₁₂ is lower alkyl, and R₁₃ is divalent alkyl radical of 2-5 carbons, or a pharmaceutically acceptable salt of said compound.

2. (Currently amended) A method in accordance with Claim 1 where X is $(C(R_{11})_2)_n$ and n is 1.
3. (Original) A method in accordance with Claim 1 where X is S.
4. (Original) A method in accordance with Claim 1 where X is O.
5. (Currently amended) A method in accordance with Claim 1 where X is NR NR'.
6. (Original) A method in accordance with Claim 1 where Y is phenyl.
7. (Original) A method in accordance with Claim 1 where Y is thiienyl.
- 8-11. (Canceled)

12. (Currently amended) A method in accordance with Claim 11 wherein said compound has a structure of formula (3) where the dashed line represents a bond.
13. (Currently amended) A method in accordance with Claim 11 wherein said compound has a structure of formula (3) where the dashed line represents a bond.

14-30 (Canceled)

31. (Previously presented) A method of treating a hypercholesterolemic mammal comprising the steps: administering to a mammal in need thereof a pharmaceutically acceptable composition comprising an FXR antagonist having the following formula



formula (3)

wherein the dashed line represents a bond or absence of a bond;

X is S, O, NR' where R' is H or alkyl of 1 to 6 carbons, or X is (C(R₁)₂)_n where R₁ is H or alkyl of 1 to 6 carbons, and n is an integer having the value of 0 to 1;

R₂ is hydrogen, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, CF₃, fluoro substituted alkyl of 1 to 6 carbons, OH, SH, alkoxy of 1 to 12 carbons, or alkylthio of 1 to 12 carbons, benzyloxy or C₁-C₁₂ alkylbenzyloxy;

R₃ is hydrogen, lower alkyl of 1 to 6 carbons or F;

m is an integer having the value of 0-3;

o is an integer having the value of 0-4 when the dashed line represents absence of a bond, and 0-3 when the dashed line represents a bond;

R'₃ is hydrogen, lower alkyl of 1 to 6 carbons, F or (R₁₅)-phenyl, (R₁₅)r-naphthyl, or (R₁₅)-heteroaryl where the heteroaryl group has 1 to 3 heteroatoms selected from the group consisting of O, S and H, r is an integer having the values of 0-5;

R₄ is alkyl of 1 to 8 carbons, or phenyl;

Y is phenyl or naphthyl group, or heteroaryl selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, imidazolyl and pyrazolyl, said phenyl and heteroaryl groups being optionally substituted with one or two R₂ groups;

s is an integer having the value of 0-2;

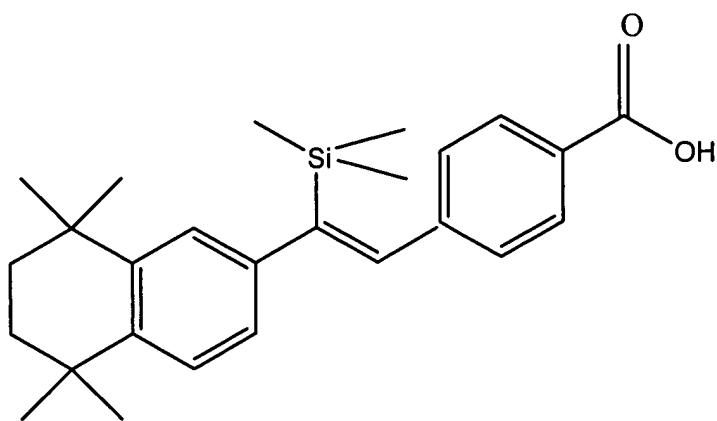
R₁₅ is independently H, F, Cl, Br, I, NO₂, N(R₈)₂, NH(R₈), COR₈, NR₈CON(R₈)₂, OH, OCOR₈, OR₈, CN, an alkyl group having 1 to 10 carbons, fluoro substituted alkyl group having 1 to 10 carbons, an alkenyl group having 1 to 10 carbons and 1 to 3 double bonds, alkynyl group having 1 to 10 carbons and 1 to 3 triple bonds, or a trialkylsilyl or trialkylsilyloxy group where the alkyl groups independently have 1 to 6 carbons;

A is $(CH_2)_q$ where q is 0-5, lower branched chain alkyl having 3-6 carbons cycloalkyl having 3-6 carbons, alkenyl having 2-6 carbons and 1 or 2 double bonds, alkynyl having 2-6 carbons and 1 or 2 triple bonds;

B is hydrogrn, COOH, NO₂, P(O)(OH)₂, P(O)(OH)OR₈, P(O)(OR₈)₂, SO₂OH, SO₂(OR₈), COOR₈, CONR₉R₁₀, -CH₂OH, CH₂OR₁₁, CH₂OCOR₁₁, CHO, CH(OR₁₂)₂, CHOR₁₃O, -COR₇, CR₇(OR₁₂)₂, CR₇OR₁₃O, or tri-lower alkylsilyl, where R₇ is an alkyl, cycloalkyl or alkenyl group containing 1 to 5 carbons, R₈ is an alkyl group of 1 to 10 carbons or trimethylsilylalkyl where the alkyl group has 1 to 10 carbons, or a cycloalkyl group of 5 to 10 carbons, or R₈ is phenyl or lower alkylphenyl, R₉ and R₁₀ independently are hydrogen, an alkyl group of 1 to 10 carbons, or a cycloalkyl group of 5-10 carbons, or phenyl or lower alkylphenyl, R₁₁ is lower alkyl, phenyl or lower alkylphenyl, R₁₂ is lower alkyl, and R₁₃ is divalent alkyl radical of 2-5 carbons, or a pharmaceutically acceptable salt of said compound.

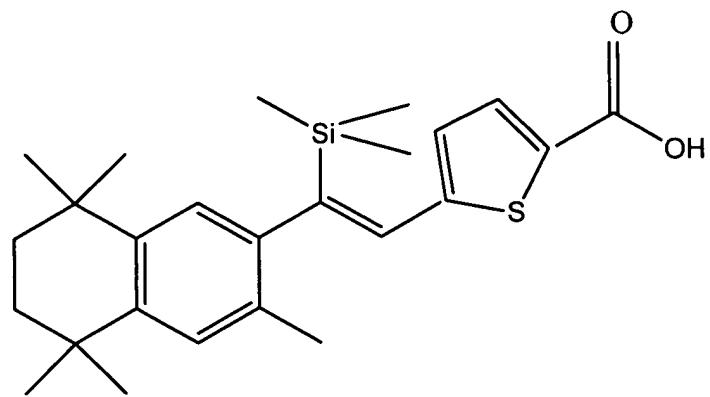
32-40 (Canceled)

41. (New) A method in accordance with Claim 1 where R₂ is H and R₄ is ethyl.
42. (New) A method in accordance with Claim 41 where B is CH₂OH.
43. (New) A method in accordance with Claim 41 where B is COOR₈.
44. (New) A method in accordance with Claim 1 where the compound of formula(3) is



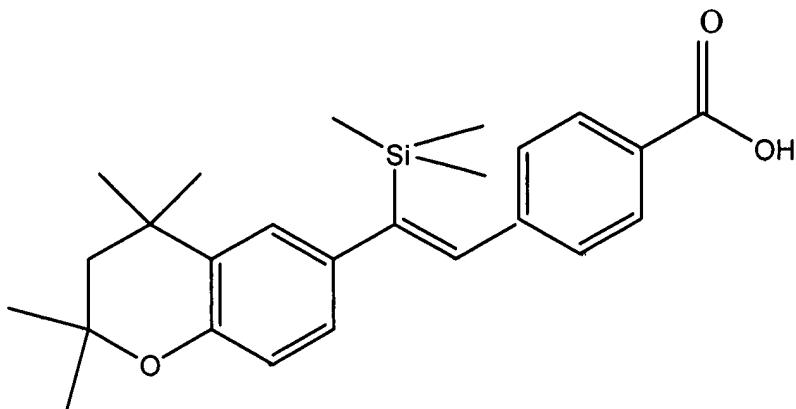
or a pharmaceutically acceptable salt thereof.

45. (New) The method in accordance with Claim 1 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

46. (New) The method in accordance with claim 1 where the compound of formula (3) is

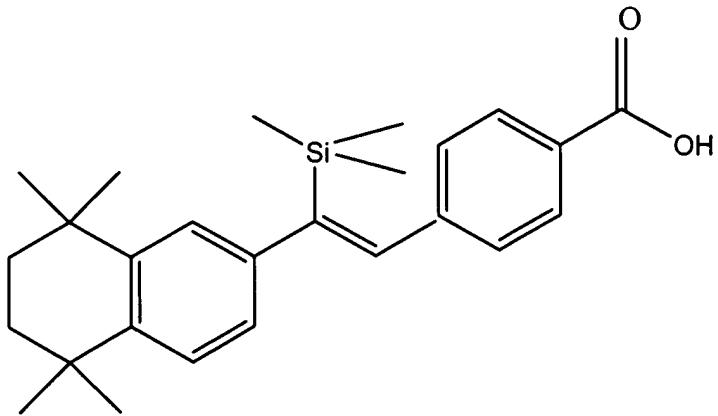


or a pharmaceutically acceptable salt thereof.

47. (New) A method in accordance with Claim 31 where R₂ is H and R₄ is ethyl.
48. (New) A method in accordance with Claim 47 where B is CH₂OH.
49. (New) A method in accordance with Claim 47 where B is COOR₈.
50. (New) A method in accordance with Claim 31 where X is (C(R₁)₂)_n and n is 1.
51. (New) A method in accordance with Claim 31 where X is S.
52. (New) A method in accordance with Claim 31 where X is O.
53. (New) A method in accordance with Claim 31 where X is NR'.
54. (New) A method in accordance with Claim 31 where Y is phenyl.

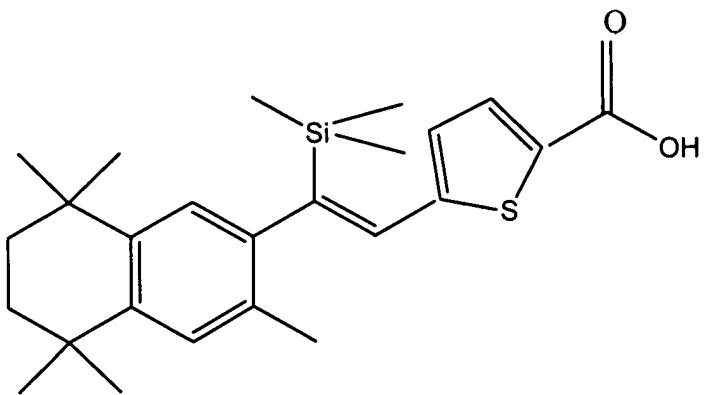
55. (New) A method in accordance with Claim 31 where Y is thienyl.

56. (New) A method in accordance with Claim 31 where the compound of formula(3) is



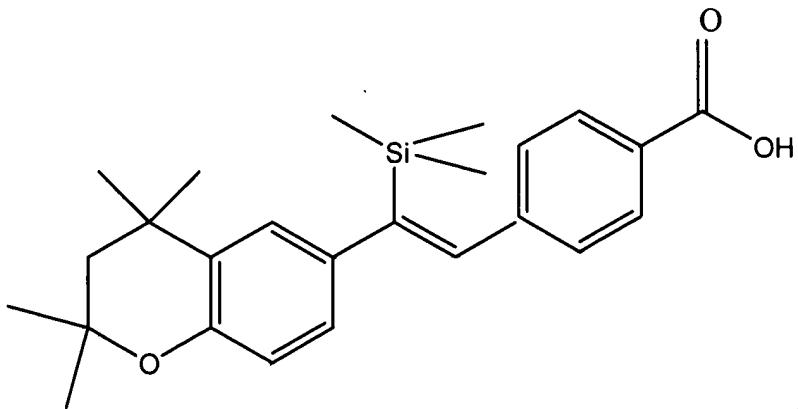
or a pharmaceutically acceptable salt thereof.

57. (New) The method in accordance with Claim 31 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

58. (New) The method in accordance with Claim 31 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

59. (New) A method of treating an FXR-mediated pathological condition selected from hypercholesterolemia and hyperlipoproteinemia in a mammal comprising the step of administering to a mammal in need thereof a pharmaceutically acceptable composition comprising (Z)-5-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trimethylsilyl)vinyl]thiophene-2-carboxylic acid.
60. (New) A method of treating a hypercholesterolemic mammal comprising the steps: administering to a mammal in need thereof a pharmaceutically acceptable composition comprising an FXR antagonist (Z)-5-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trimethylsilyl)vinyl]thiophene-2-carboxylic acid.